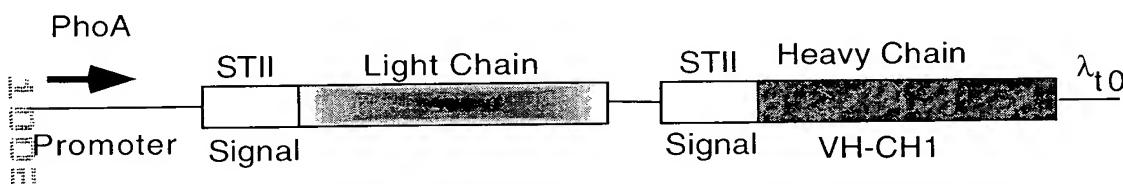


Fab Expression Vector pAK19



Full Length Antibody Expression Vector Derived from pAK19

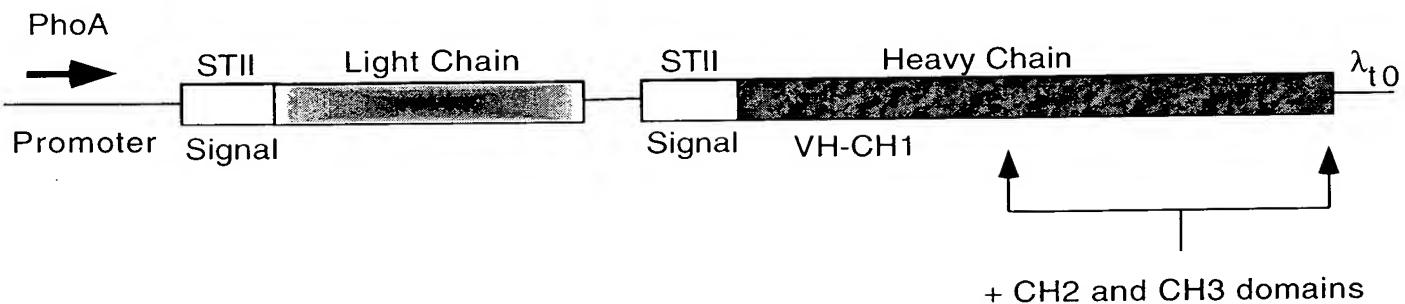


Figure 1

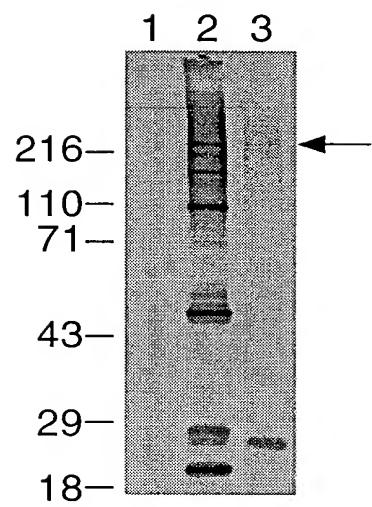


Figure 2

## Polycistronic Constructs

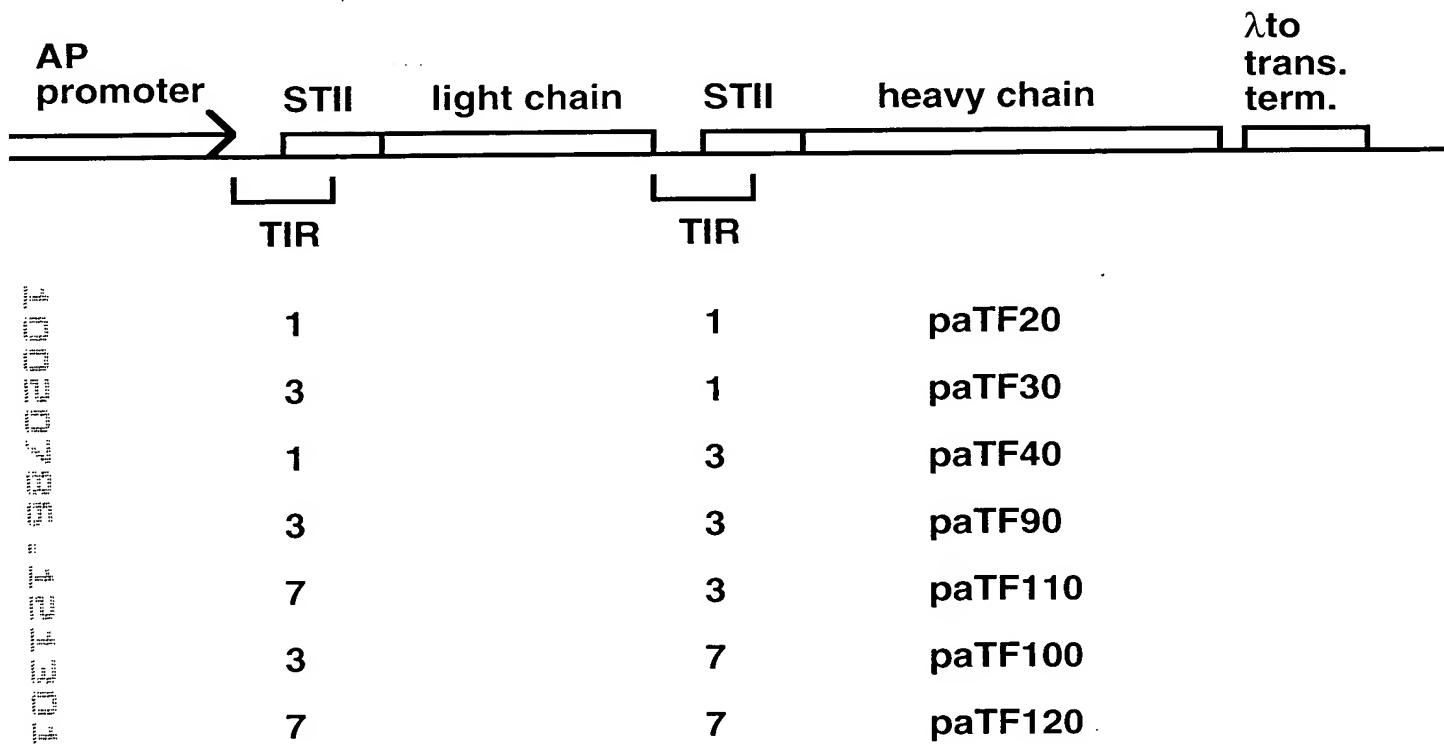
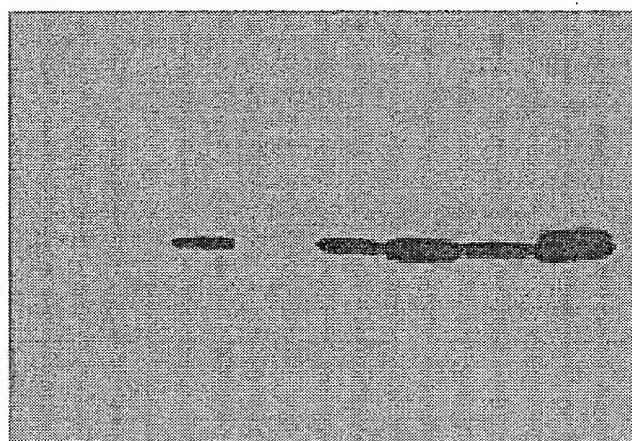


Figure 3.

polycistronic  
reduced

neg. 1L 3L 1L 3L 7L 3L 7L  
1H 1H 3H 3H 3H 7H 7H

4A



— heavy

— light

polycistronic  
non-reduced

neg. 1L 3L 1L 3L 7L 3L 7L  
1H 1H 3H 3H 3H 7H 7H

4B

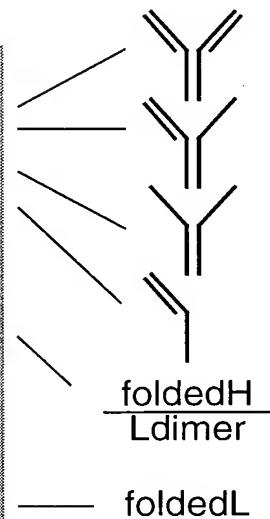
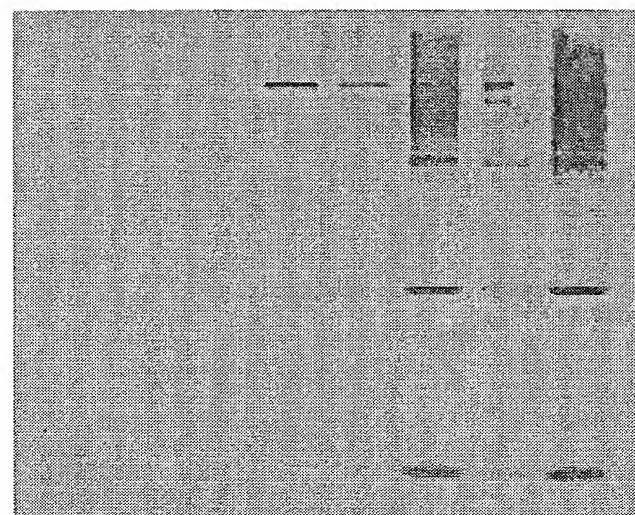
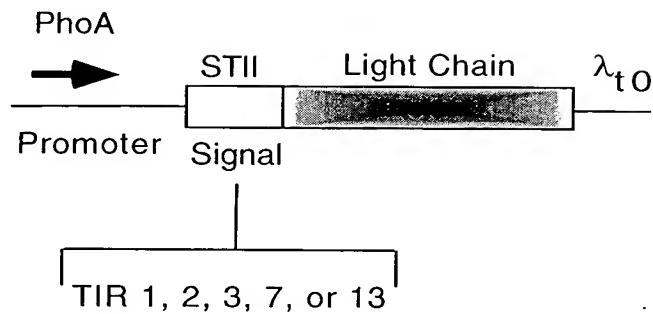


Figure 4

### Light Chain Constructions



### Heavy Chain Constructions

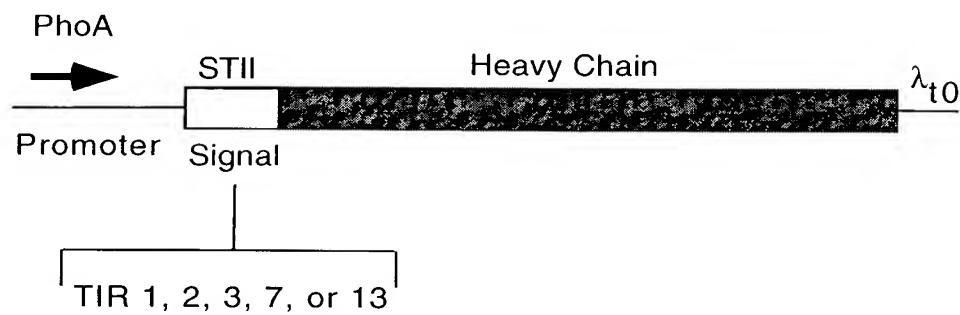


Figure 5

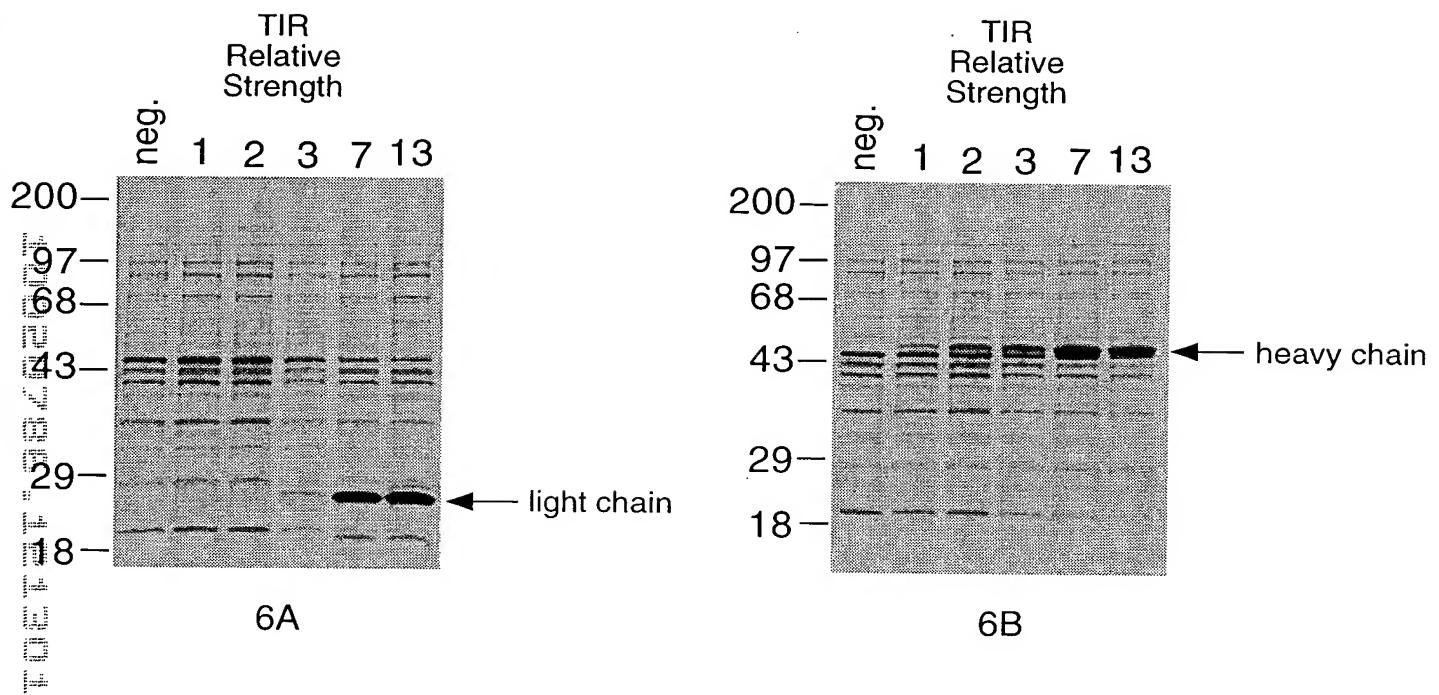


Figure 6

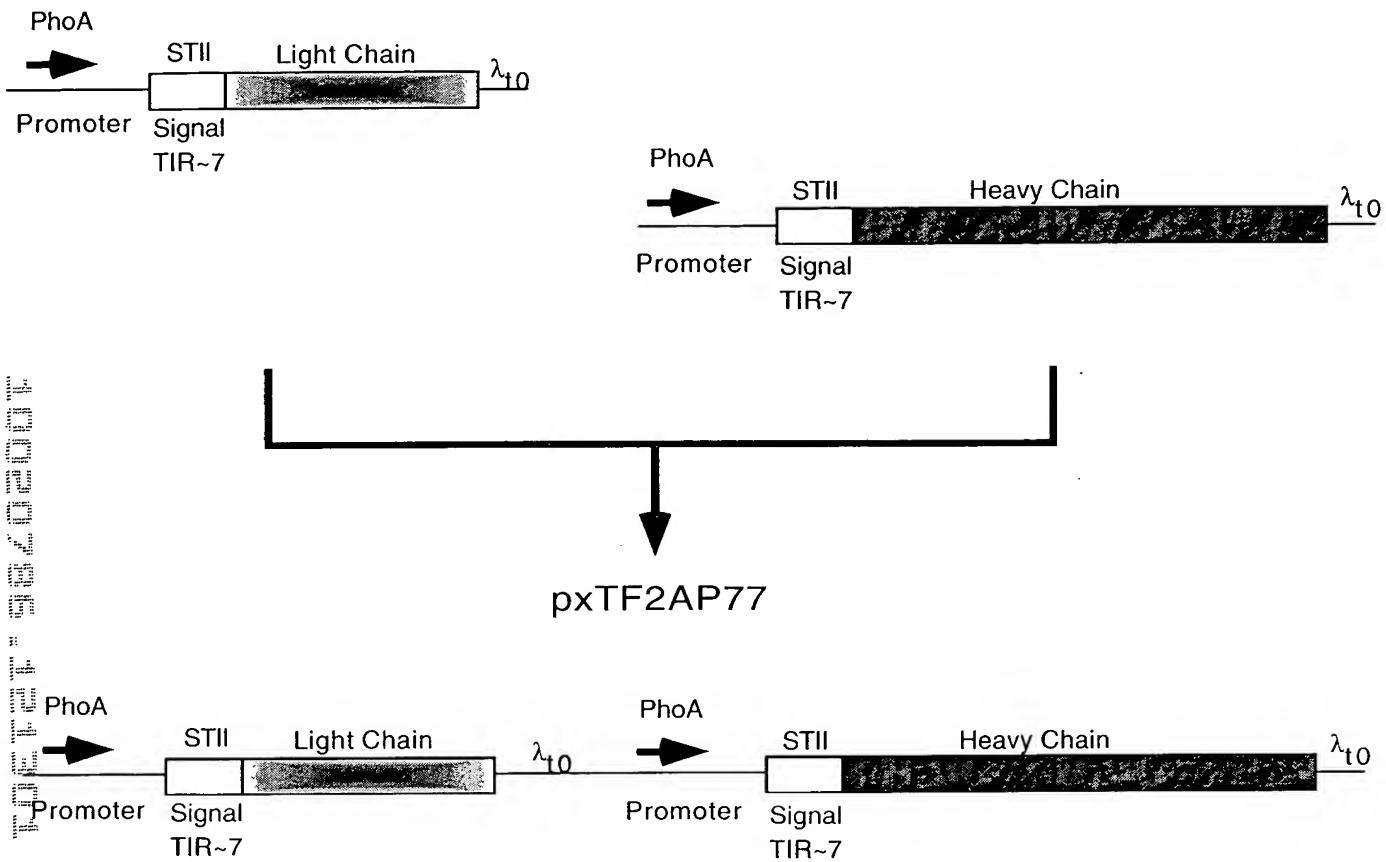


Figure 7

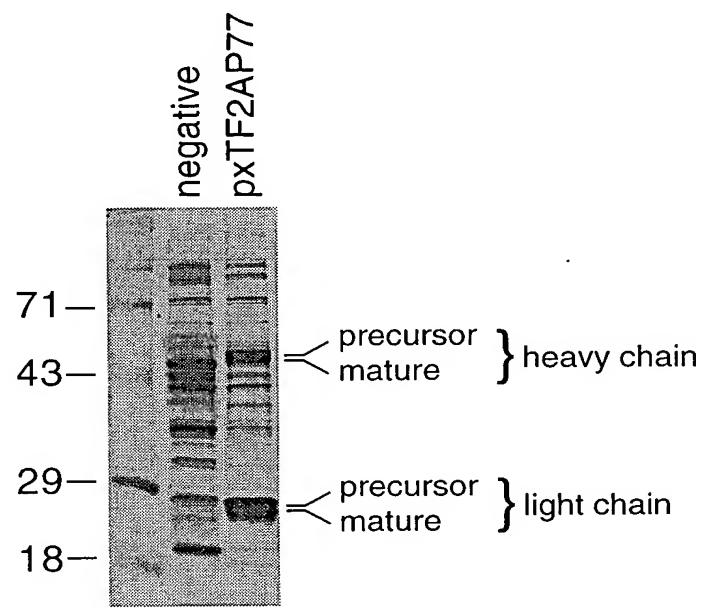


Figure 8

## Separate Cistron Constructs

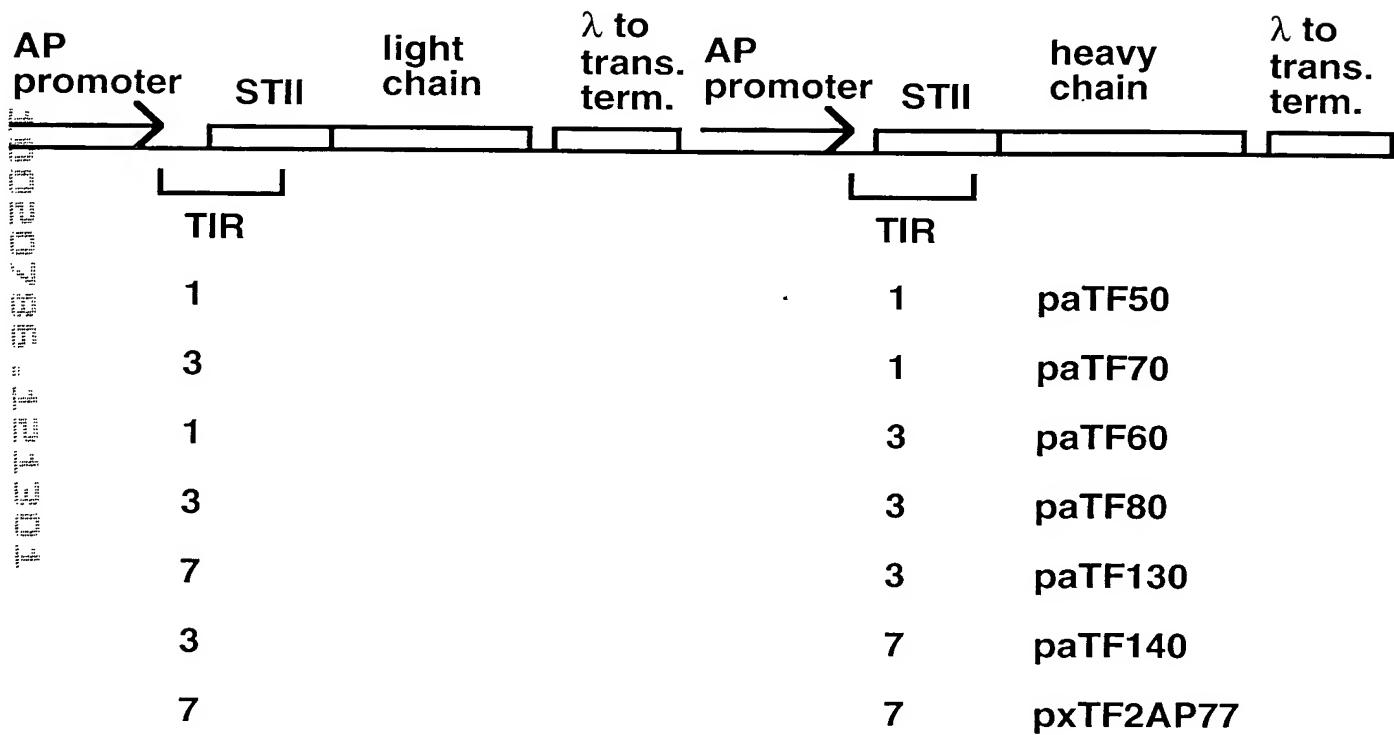


Figure 9

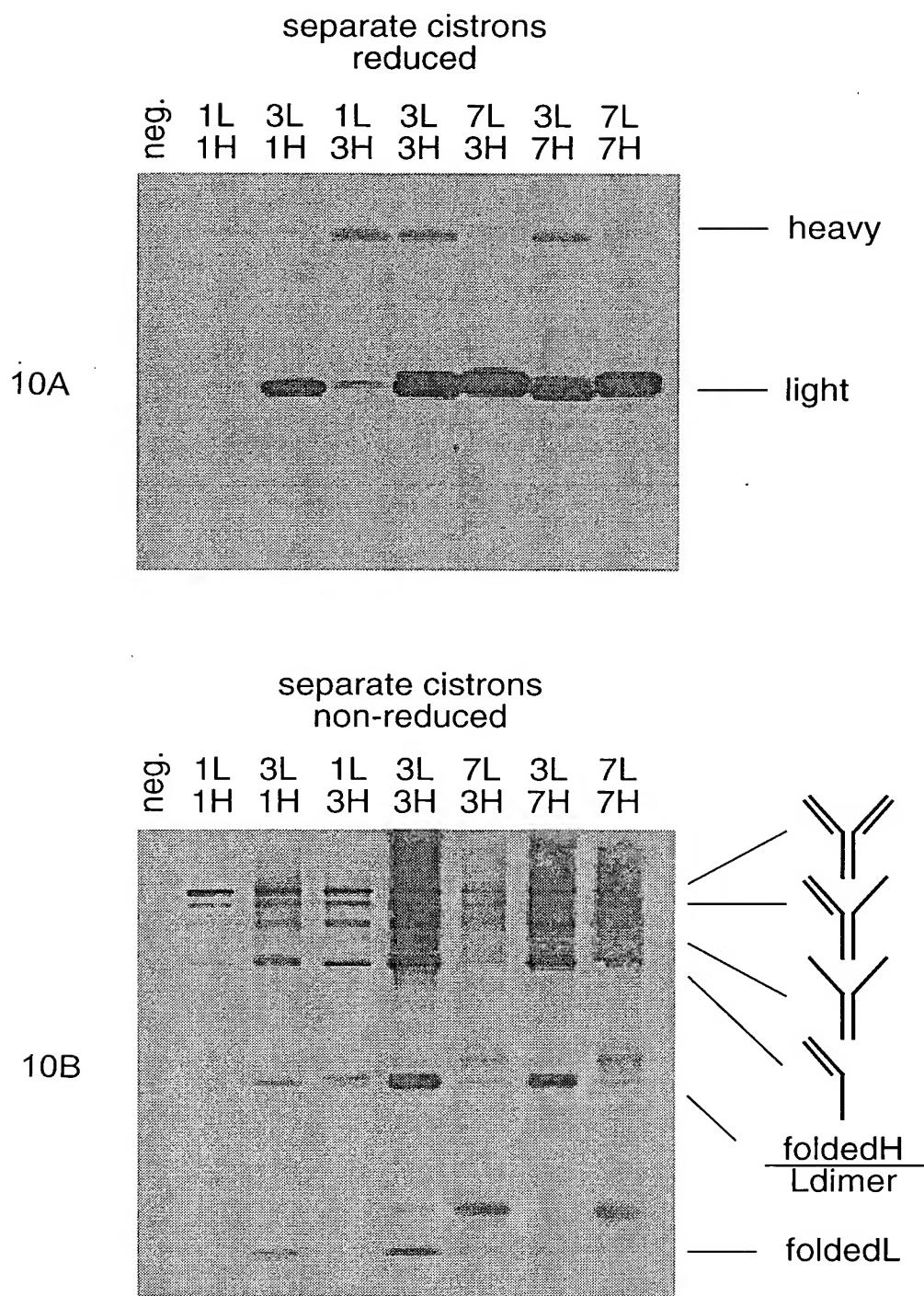
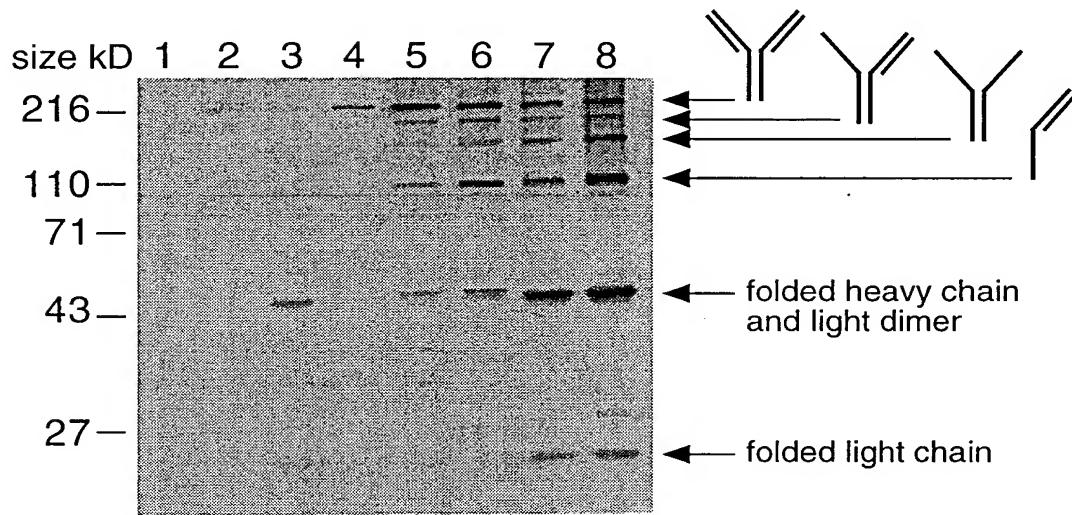


Figure 10



- 1) negative control
- 2) TIR 1-light, TIR 1-heavy, polycistronic
- 3) TIR 3-light, TIR 1-heavy, polycistronic
- 4) TIR 1-light, TIR 3-heavy, polycistronic
- 5) TIR 1-light, TIR 1-heavy, separate cistrons
- 6) TIR 1-light, TIR 3-heavy, separate cistrons
- 7) TIR 3-light, TIR 1-heavy, separate cistrons
- 8) TIR 3-light, TIR 3-heavy, separate cistrons

Figure 11

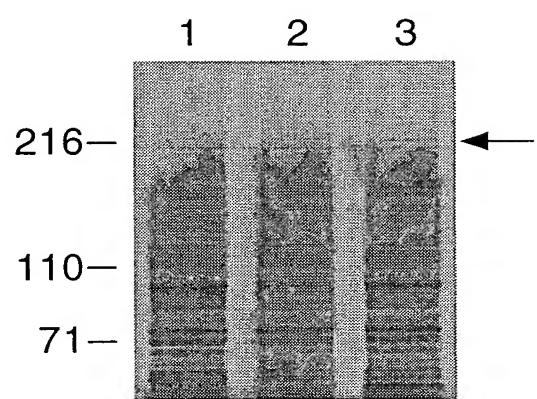


Figure 12

...  
...  
...  
...  
...  
...

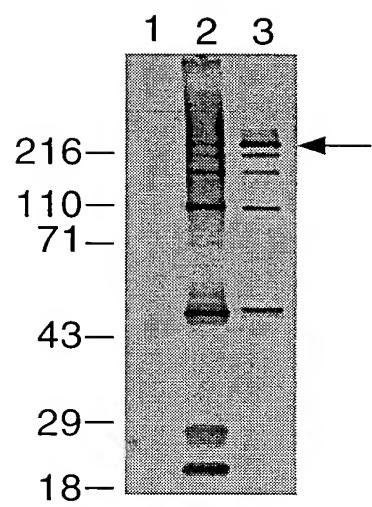


Figure 13

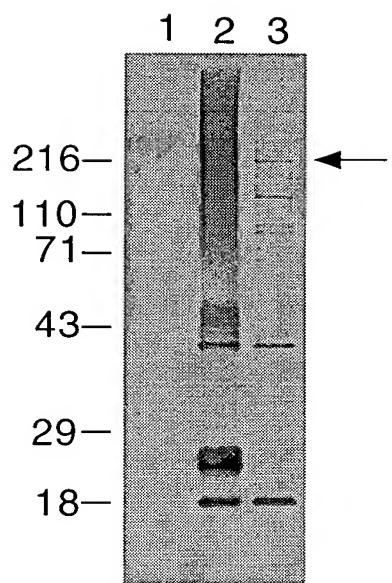


Figure 14

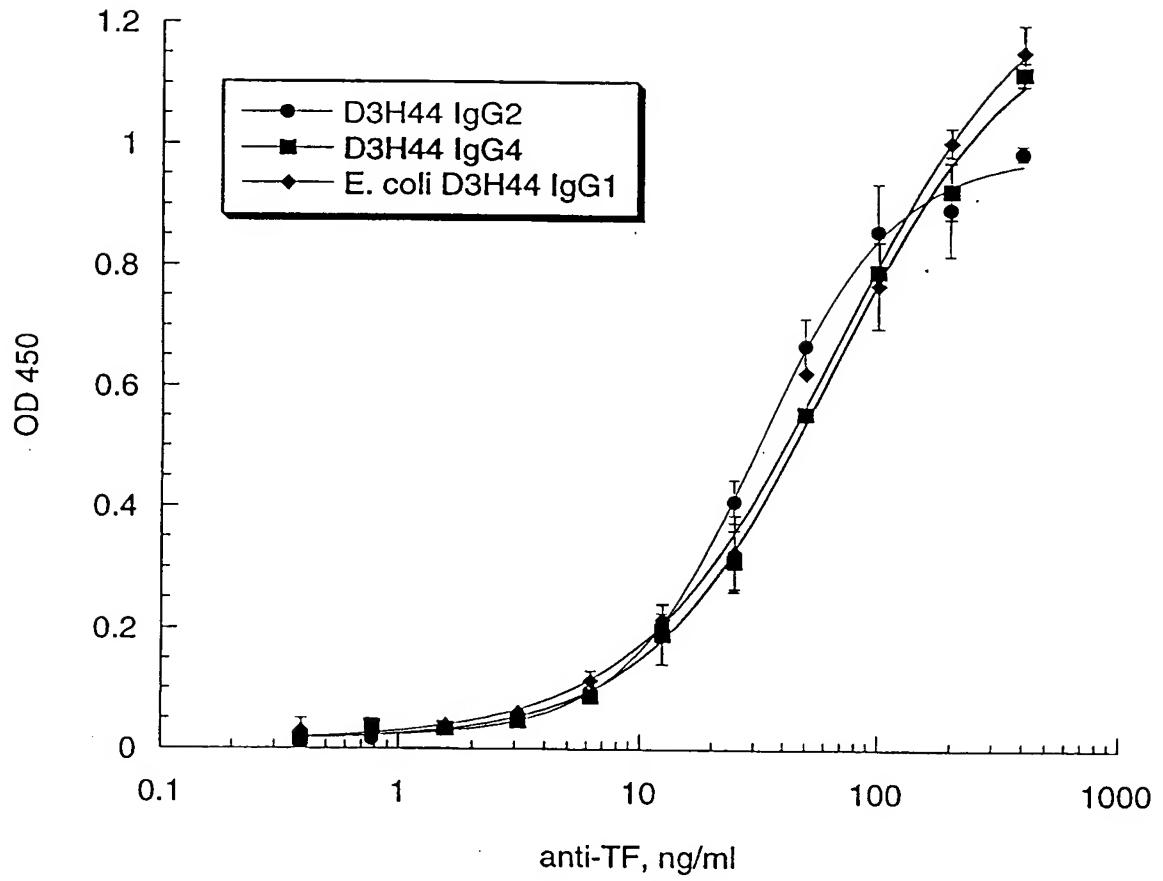


Figure 15

100 90 80 70 60 50 40 30 20 10

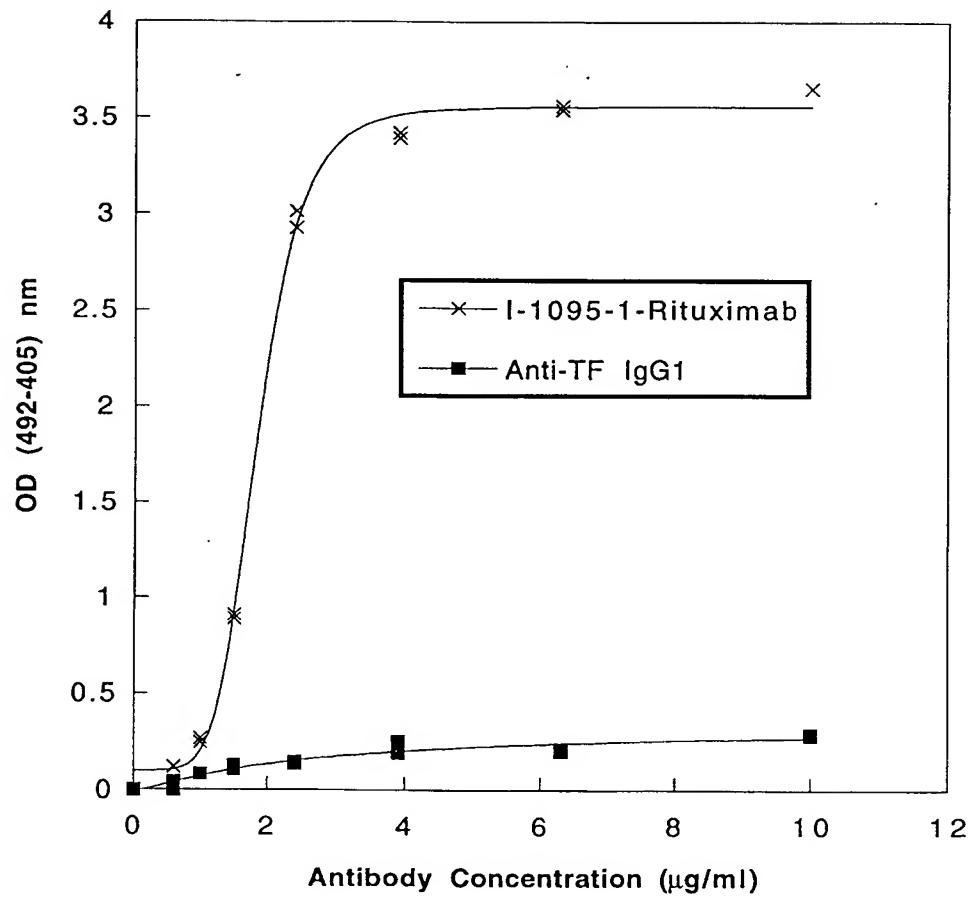


Figure 16

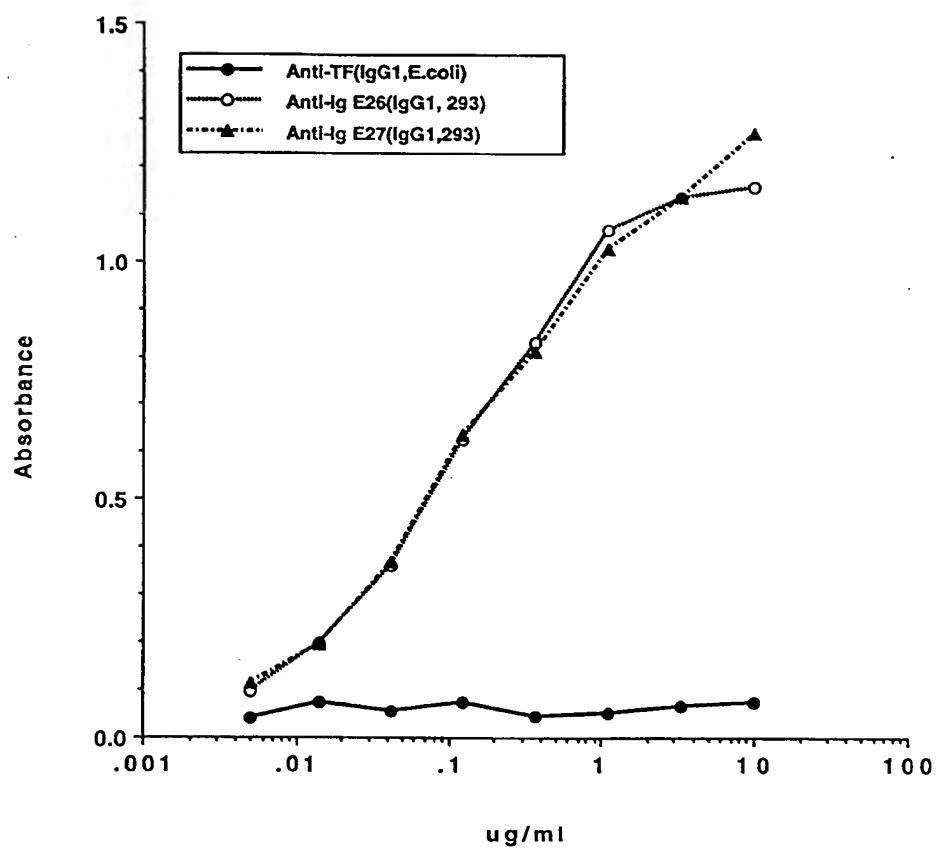


Figure 17

O.D. @ 450nm

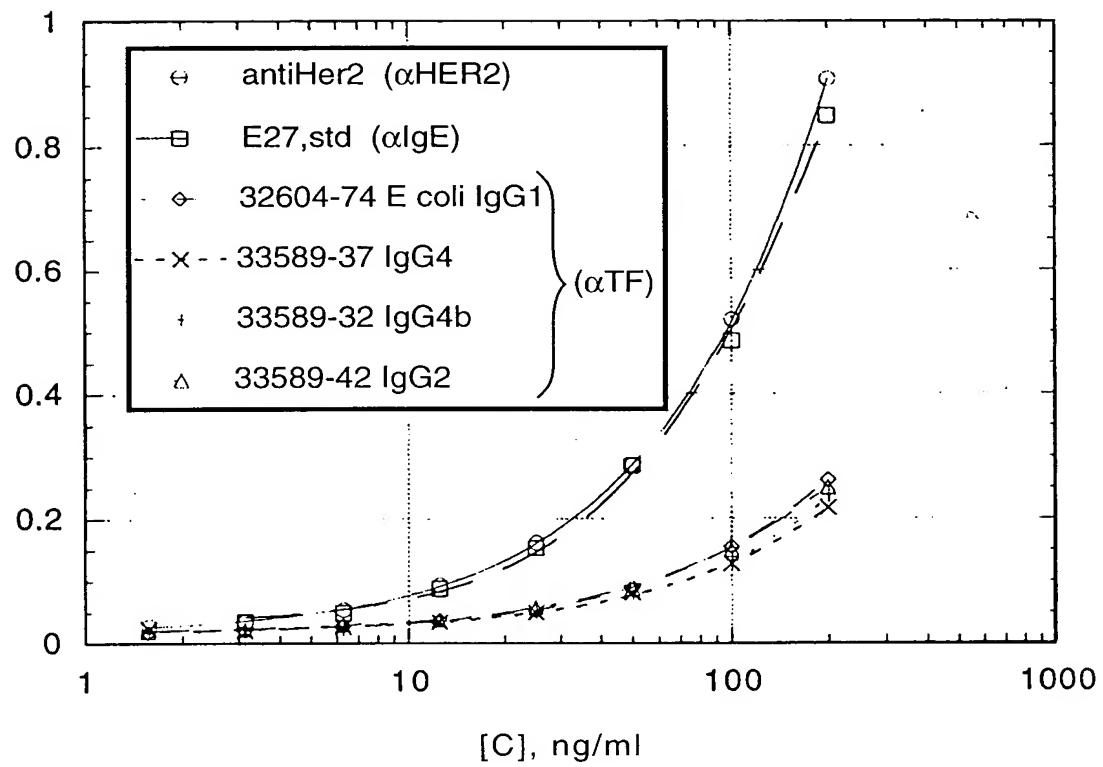


Figure 18

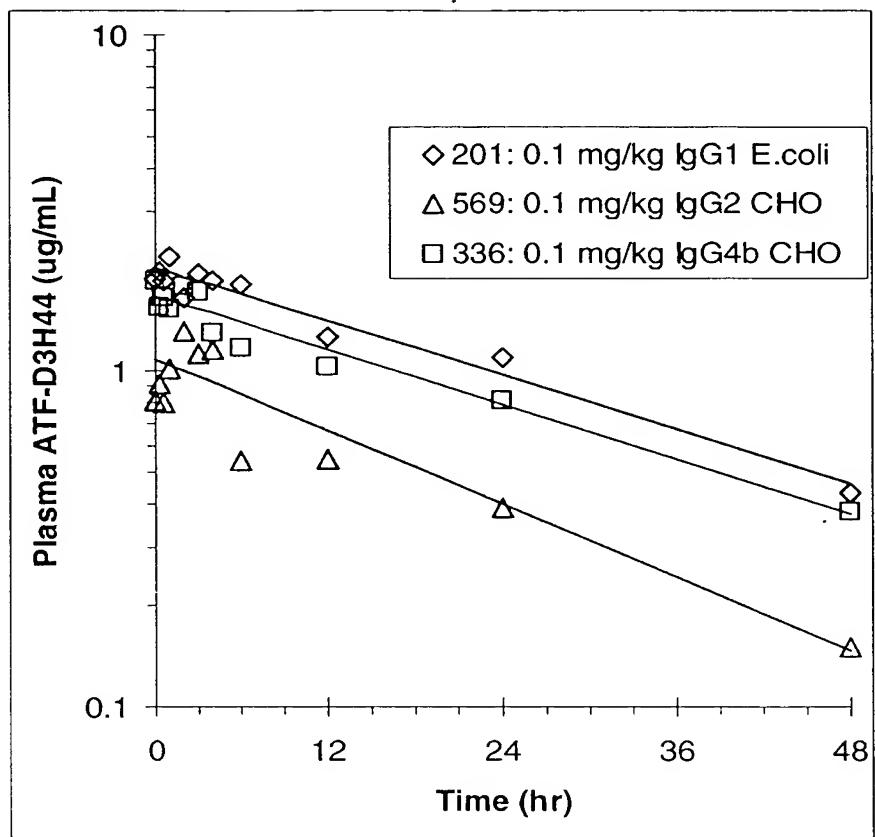


Figure 19

1 GAATTCAACT TCTCCATACT TGGATAAGG AAATACAGAC ATGAAAATC TCATTGCTGA GTTGTATT AAGCTGCC AAAAGAGA AGAGTCGAAT  
 CTTAATGTA AGGGATGAA AACCTATTC TTATGTCG TACTTTAG ATGAACTG ACTTATG 101  
  
 101 GAACTGTG CGCAAGGTASA AGGTTGAG ATTATGCTCA CTGAAATGCT TCGAAATGTC TCGAAATG ACCAACAGGG GTGATGAT CAGGTAGG  
 CTTGACACAC GCGTCATCT TCGAAACCTC TATAGCTAGT GACGTACCA AGCGTATAC CGCGTTTAC TGGTGTCC CHACTAATCA GTCCATCTCC  
  
 201 GGGCGCTGTA CGAGSTAAG CCCGATGCCA GCATTCTGTA CGACGATACG GAGCTGTGC GCGATTACG AAACAGGTTA TGAAGGATC CTCGTGATA  
 CCCGGACAT GCTCCATTIC GGCTACGGT CGTAAGGACT GCTGTATGC CTGACGAGC CGCTAAATGCA TTTCCTCAT AACTCGTGAGC GAGCACTAT  
  
 301 AAAAGTTAT CTTTCAACA GCTGTCTAA ACTTGTCAAG CGCGAGACTT ATAGTCGTT TGTGTTAT TTGTAATGTA TTGTAACCA GTACGAAAT  
 TTTCAATTA GAAAGTGTG CGACGTTATC TCAACAGTGC CGGCTCTGAA TATAGCAGAA ACAAAATAA AAAATTACAT AAACATGAT CATGCGTCA  
  
 401 TCACCTAAAA AGGGTATCPA GAATTGATAA GAAGAATATC GCATTTCTC TTGATCTAT GTTCGTTTT TCTATTGCTA CAAACGCCA CGCTGATAATC  
 ATGCAATTTC TCCCAGTAGAT CTAAATACTT CTCTCTATAG CGTAAAGAAG AACGCTAGATA CAAGCAAAA AGATAACGAT GTTGTGGAT GCGACTATAG  
 1 M K K N I A F L L A S M F V F S I A T N A Y A D I  
 ^SII Signal Sequence TIR-1  
 Anti-Tissue Factor Light Chain^

501 CAGATBACCC AGTCCCCGAG CTCTCTGTC GCCTCTGG GCGATAGGGT CACCATCAC TGAGAGCCA GTCGGACAT CAGAGCTAT CTGAACCTGT  
 GTCTACTGGG TCAGGGGCTC GAGGACAGG CGAGACACC CGCTATCCCA GTGCTAGTG AGCTCTCGGT CAGGCTGATA GACTTGACCA  
 26 Q M T Q S P S S L S A S V G D R V T I T C R A S R D I K S Y L N W Y  
  
 60 ATCAAAGAA ACCAGAAA GCTCCGAGA TACTGTTTA CTATGCTACT AGTCTCGCTG AAGGACTCC TCCTCGCTC TCDGGATCC GTTCTGGAC  
 TAGTGTCTT TGGTCTTCTT CGAGGCTTCTT ATGACTAAAT GATAGCTGTA TCAGGCGAC TTCTCTAGGG AAGACCGAG AGACCTAGC CAAGACCTG  
 60 Q Q K P G K A P K V L I Y Y A T S L A E G V P S R F S G S G T  
  
 701 GGATTAACCT CTGACCATCA GCAGCTGCA GCCAGAAGAC TTCGAAACTT ATTACTGTCT TCAGCACGGA GAGTCCTCAT GGACATTGG ACAGGGTACCC  
 CCTAAATGTA GACTGTGTTGCTGAGCT CGTCAAGACT CGTCTCTGTA AGGCTGTGAA TAATGACAGA ACTCGTGCCT CTCAGAGTA CCCTAAACG TSTCCCTGG  
 93 D Y T L T I S S L Q P E D F A T Y Y C L Q H G E S P W T F G Q G T

801 AAGGTGGAGA TCAAACGAC TGTGGCTGCA CCATCTGCT TCACTCTCCC GCCATCTGAT GAGGAGTGA AATCTGGAAAC TGCTCTCTT GTGTGCTG  
 TTCCACCTCT AGTGTGTTG ACACCGACTT GGTAGAGAGG CGGTAGACTA CTGTCACCT TTAGACCTG AGCAAGAAA CACACGAGC  
 126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATAACCT CTATCCAGA GAGGCCAAG TACAGTGAA CGTGGATAAC GCCCTCCCAT CGGTAACCTC CCAGGAGGT CTCAGAGGT GTCACAGAGC AGGACAGCAA  
 ACTTATGAA GATAAGGTCT CTCGGTTCT ATGTCACCTT CCACCTATTG CGGAGGTTA GGCATGAG GGTCTCTCA CAGTGTCTG TCCTGTGCTT  
 160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

1001 GGACAGGACCC TACAGGCTCA GCAGCACCTC GAGGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGCTAC GCCTGGAAAG TCACCCATCA GGGCTGAGC  
 CCTGTGCTGG ATGTCGGAGT CGTCTGGGA CTGCGACTCG TTTCGCTCTGA TGCTCTTGT GTTCGATG CGGAGGCTC AGGGGTAT CCCGGACTCG  
 193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V V T H Q G L S

1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGAA GAGGTAAAT TAATCCTCT ACGCCGGAGG CTCGTTGGGAGG AGCTCGGTAC CCGGGATCT AGGCCTAACG  
 AGCGGGCAGT GTTGTCTGAA GTTGTCTCCCT CTGAGCCCTCG TGCCTCCCTC GTAGCACGGC TGAGCCCTAGA TCGGGATG

226 S P V T K S F N R G E C O

Figure 20a

1201 CTCGCGTTGCC GCGGGGGCTT TTTTATTGTT GCCACCGGGC ATCTCGAATG AACTGTGTC GCAGGGTAGA GTTGGGAGA TTATCGTCAC TGCATGCTT  
 GAGGCAACCG CGGCCCGCAA AAAATACAA CGCGTGGCG TTAGCTAC TTGACGACG CGTCATCTT CGAACCTCTT ATAAGTAGTG AGTTACGAA  
 1301 CGCAATATGG CGAAATAGA CCAAACRGCGG TTGATTGATC AGSTAGGGG GGCCTGTCAC GAGGTAAAGC CGCATGCC CATCCGAC GACGATACGG  
 GCGTTATACC GCGTTTACT GGTGTCGCC AAATACTAG TCCATCTCC CGCGACATG CTCCATTG GGTCAGGTG TAAGGACTG CTGCTATGCC  
 1401 AGCTGCTGG CGATTAGTA AAGAAGTAT TGAGACATC TCGTCATCAA AAAGTAACTC TTTCACAG CTGTCATCAA GTTGTACGG CGAGACITTA  
 TCGAGACCC GCTAATGCT TTCTCAATA ACTCTGTAAG AGCTGATT TTTCATTAG AAANGTTGIC GACAGTATT CAACAGTGCC GGCTGTAAT  
 1501 TAGTGCTT GTTTTATT TTAATGTT TGTAACTAG TAGGCAAGT AACGTTAAAGA GGGTACTAG AATTATGAG AAGAAATATCG CATTTCCTCT  
 ATCAGCGAAA CAAAATAAA AAATTACATA AACATTGATC ATGCGTCAA GTGCAATTTC CCCATAGATC TAAATAC TCTATAGC GTAAAGAAGA  
 1 ^ST11 Signal Sequence TIR-1

1601 TGCATCTATG TTGTTTTCTT CTATGCTAC AAAGGGTAC GCTGAGGTTT AGCTGGGGA GTCTGGGG AGCCAGGGG CTCACTCCGT  
 ACGTAGATAC AGGCAAAAAA GATAACGATG TTTCGCTATG COACTCAAG TGACCAACCT CAGACGCCA CGCGACACG TGCGTCGCC GAGTGAGGCA  
 10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R  
 ^Anti-Tissue Factor Heavy Chain

1701 TTGCTCTG CAGCTTCTGG CTCATATAATTAAGGAGTACT ACATGCTCTG GGTCCTCTAG GCCCGGGTA AGGGCCTGGA ATGGGTTGGA TTGATTGATC  
 AACGGACAC GTGAGAAC GAAAGTAA TTCTCTGAGA TGATGCGAC CGAGGACTC CGGGGCCAT TCCGGACCT TACCCACCT AACAACTAG  
 43 L S C A A S G F N I K E Y Y M H W V R Q A P G K G L E W V G L I D P

1801 CAGGCGAAGG CAACACATC TATGACCGA AGTTCAGGA CGGTGCACT ATAAGGCTG ACAATTCMA AAACACAGCA TACCTCAGA TGAACAGCCT  
 GTCTCGTCTC GTTGTGCTAG ATACTGGCT TCAAGGCTCT GGCACGGTA TATTCCGAC TGTAAAGTT TTGTTGCTGT ATGAGGCTT ACTGTCGGA  
 77 E Q G N T I Y D P K F Q D R A T I S A D N S K N T A Y L Q M N S L

1901 GCGTGTGAG GACACTGCCG TCTATTATG TGCTCGAGAC AGGGCCCTT ACTTCGACTA CTGGGTCA GGAAACCCCTGG TCACCGCTCTC CTGGCCCTCC  
 CGCACGACTC CTGTGAGGCC AGATAATAAC ACGGACTCTG TGCCGGAA TGAAGGTGAT GACCCAGTT CCTTGGGACCT AGTGGAGAG GAGCGGGAGG  
 110 R A E D T A V Y Y C A R D T A A Y F D Y W Q G T L V T V S S A S

2001 ACCAAGGGCC CATCGGTCTT CCCCTGGCA CCCTCCTCCA AGAGCACCTC TGGGGCACA GCGGCCCTGG GCTGCCCTGG CAAGGACTAC TTCCCCGAAAC  
 TGGTTCGG GTAGCCAGAA GGGGACCGT TCTCGTGGAG ACCCCGGTGT CGCGGGGACCA GTTTCCTGATG AAGGGGCTG  
 143 T K G P S V F P L A P S S K S T S G G T A A L G C L V K D Y F P E P

2101 CGTGTGACGT GTCGTGAAAC TCAGGGGCC TGACCGGG CGTGCACCC TTCCCGCTG TCCTACAGTC CTCAAGGACTC TACTCCCTCA GCAGGGGGTT  
 177 V T V S W N S G A L T S G V H T F P A V L Q S S G L Y S L S S V V  
 GCCACTGCA CAGCACCTG AGTCGGGG ACTGTCGCC GCACGTGTT AAGGGCGAC AGGATGTCAG GNGTCCTGAG ATGAGGAGT CGTCGACCA  
 CTGACACGG AGATCGTGA ACCCGTGGGT CTGATGTAAGTGGACT TAGTGTGTCAG GCTGCTGAG TCCACCTGT TCTTCACCT CGGGTTTGA  
 2201 GACTGTGCC TCTAGGAGCT TGGGACCCA GACCTACATC TCGAACCTGA ATCACAGCC CAGAACACC AGAAAGTGA GCCTAACATCT  
 210 T V P S S S L G T Q T Y I C N V N H K P S N T K V D K K V E P K S

2301 TGTGACAAAA CTCACACATG CCCACCGTGC CCAGCACCTG AAECTCTGG GGGACCGTCA GTCTCCCTCT TCCCCTAAA ACCAACAGGAC ACCCTCATGA  
 243 C D K T H T C P P C P A P E L L G G P S V F L F P P K P K D T L M I  
 ACATGCTT GAGTGTGTCAC GGTTGCGACG TTGAGGACCC CCCTGCGAGT CAGAGGAGA AGGGGGTTT TGGTGTCTG TGGGAGTACT  
 2401 TCTCCGGAC CCCTGAGGTC ACATGCTGG TGGGGAGGT GAGCCAGGA GACCCCTGAG TCAAGGTTCAA CTGGTAGCTG GACGGGGTGG AGGTGCTAA  
 AGAGGGCTG GGGACTCAG TGTAGGCC ACCACCTGA CTGGGTCTT AGTCAAGT GACATGACCT CTGGGACCC TCCAGTATT  
 277 S R T P E V T C V V V D V S H E D P E V K F N W Y V D G V E V H N

Figure 20b

Start Tet Resistance Coding Sequence

2501 TGCCTAGACA AAGCCGGGG AGGAGCACTA CAACAGGACG TACCGTGTGG TCAGCGTCCT CACCGGACT CACCGTCTG GGCCTGAATGG CAAGGGTAC  
ACGGITCTGT TTGCGGCC TCCITCGTAT GTTGTCTGC ATGGCACACC AGTGCAGAAC GTCGCAAGAC GTGGCAGAAC GTGGCTCTGA CGCAGTCTACG  
310 A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W L N G K E Y  
2601 AAGTGCAGG TCTCCAACAA AGCCCATCG AGAAAACCAT CTCCAAGGCC AAAGGGCGC CCCGAGAAC ACCCTGTTAC ACAGGTGTA  
TTCACGTTCC AGAGTTGTT TCGGAGGTT CGGGTAGC TCTTGTGA GAGGTTCGGS TTTCCTCG GGGCTCTGG TGTCACATG TGGGACGGG  
343 K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q V Y T L P P  
2701 CATCCCGGA AGAGATGACC AGAACCCAG TAGCCCTGAC CTGCGCTGGC AAAGGCTTT ATCCAGGA CATCGCGTG GAGTGGAGA GCAATGGCA  
GTAGGGCCCT TCTCTACTGG TTCTGGTCC AGTCGACTC GACGGACCAAG TTTCGAAAGA TAGGGTGTCT GTAGCGCAC CTCACCTCT CGTTACCGT  
377 S R E E M T K N Q V S L T C L V K G F Y P S D I A V E W F S N G Q  
2801 GCGGAGAAC AACTACAAGA CCAAGCTCC CGTGTGGAC TCCGAGGGCT CCTCTCTCT CTACAGNAG CTACCGTGG ACAAGAGAG GTCGAGCAG  
CGGCCCTCTG TTGATGTTCT GTGGTGTCT CGACGACTCT AGGCTGCCGA GGAAAGAAGA GATGTCGTC GAGTGGCAC CTCACCGTGC  
410 P E N N Y K T T P P V L D S D G S F F L Y S K L T V D K S R W Q Q  
2901 GGGAAAGTCT TCTCATGCTC CGTGTATGGCAT GAGGGCTCTGC ACAACCACTA CACCGAGAG AGCCTCTCC TGTCCTCGG TAAATAAGCA TGGGACGGCC  
CCCTTCAGA AGAGTAGAG GCACTACTA CTCCGAGACG TGTGTGTGAT GTGGCTCTC TGCGAGGGG ACAGGGCCC ATTATATCTG AGCTGCGGG  
443 G N V F S C S V M H E A L H N Y T Q K S L S P G K O  
3001 CTAGACTCCC TAACCCCTCGG TTGCGCGGG GGGTTTTTA TTGTTAACTC ATGTTGAGCA GTTGTATCATC GATAAGCTTT AATGGCTGG TTATACAG  
GATCTAGGG ATTGGAGCC AACGGAGCC CGCRAAAAT AACAAATTGAG TACAAACTGT CGAATAGTAG CTATTGAAA TTAGGCATC AAATACTGTC  
3101 TTAATTGCT AACGGAGTCA GGACCCGTG ATGAAATCTA ACAATGCGCT CATGGTCATC CTGGCACCG TCACCCCTGG TGCTGTAGC ATAGGCTGG  
AATTAACGA TTGCTCTAGT CCTGGCACTA TACTTATGAT TTGTTAGCA GTACCAAGAG AGTGGACCT ACGACATCG TATCCGACCC

3201 TTATGCCGGT ACTGCCGGG CTCTTGGGG ATATCGTCCA TTCCGACAGC ATCGCCAGTC ACTATGGGT GCTGCTAGG CTATATGGT TGATGGATT  
AATACGCCA TGA CGCCCG GAGAACGCC TATAGCAGG TAGGGTGTGG AAGGTAGGT GATAACCGA CGACGATCG GATAACGCA ACTACGTTAA

Figure 20c

1 GAATTCACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAATC TCATGCTGA GTTGTATT AAGCTGCC AAAAGAAGA AGAGTCGAAT  
 CTTAAGTGA AGAGGTATGA AACCTATTC TTTATGCTG TACTTITAG AGTAAGCAT CAACATAAA TTGAAAGGG TTITTCCTC TCTAGCTTA  
  
 101 GAACTGCTG CGCAAGTAGA AGCTTGGG AGTATCGTA CTGCAATGCT TCGCATATG GCACAAATG ACCAACAGG GTTGATGAT CAGTAGG  
 CTTGACACAC CGTGTCCATCT TCGAAACCTC TAATGCGT GACGTCAGA AGCGTTATAC CGCGTTTAC TGTTGTCGC CAACTA CTC  
  
 201 GGGCGCTTA CGAGGTAAG CCAGATGCCA GATTCCTGCA GAGCAGATAC GAGCTGCTGC GCGATTACG AAAAGACTA TTGAGCATC CTCGTCAGTA  
 CCCGCGAGAT GTCGCCATTC GGCTGACGGT CTAGGAGCT GTGCTPATGC CTGCGAGGCG CGTAAATGCA TTTCCTCAT AACTCTGAG GAGGAGCT  
  
 301 AAAGTTAT CTTTAAACA GCTGTCAAAGGTTGCTACG GCGGAGACTT ATAGTCGCTT TGTTTTATT TTAAATGTA TTGTAACTA GTACGCCAGT  
 TTTCATTA GAAAGTGTG CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATCGCTCA  
  
 401 TCACGTAAA AGGGTATCTA GAATTATGAA GAGAAATTC GCAATTCTTC TTGCACTCAT TTGCTGTTTCTA CAAACGCCGA CGCTGATATC  
 AGTGCTTTC TCCATAGAT CTAAACTC CTICCTATAG AACGPAGATA CAACCCAAA AGATAACGAT GTTTCGGCAT GCCACTATAG  
 1 M K K N I A F L L A S M F V F S I A T N A Y A D I  
 \*STII Signal TIR -1 Anti-VEGF Light chain^

501 CAGTGACCC AGTCCCCGAG CTCCCTGTC GCCTCTGTGG GGATGGGT CACCATCACCG TGAGCGGA GTCAAGGATAT TAGCAACTAT TTAACCTGTT  
 GTCAACTGG TCAGGGGCTC GAGGGACAGG CGGAGACAC CGCTATCCCA GTGGTAGTGG ACGTGCGST CAGTCCTATA ATCGTGTATA AATTGACCA  
 26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y  
  
 60 ATCAACGAA ACCAGAAA GCTCCGAAG TRCTGRTTA CTTCACCTCC TCTCTCCTACT CTGGAGTC GCCTCGCTTC TCTGATGCG GTTCTGGGAC  
 TAGTGTCTT TGGCTTTT CGAGGCTTC ATGACTAAAT GAAAGTGGGG AGAGGGTGA GACCTCAGG AGACCTGGC CAAGACCTGC  
 60 Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T  
  
 701 GGATTGACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTGCGAACTT ATTACTGCTA ACAGTATAG ACCGTGCCGT GGACGTTTG ACAGGTAC  
 CCTAAAGTGA GACTGTAGT CGTAGACCT CGCTCTCTG AGCGTGTGAA TAATGACACT TGTCATATG TGCCATCTGAA CCTGCAAAAC TGTCCTCTGG  
 93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T  
  
 801 AAGGTTGAGA TCAAACGAAC TTGTGCTGCA CCATCTGCT TCATCTTCCC GCCATCTGAT GAGCAGTGA AAATCTGGAA ACCTGCTGTT GTGTGCTG  
 TTCCACCTCT AGTGTGCTG ACCGAGCT GTAGAGAGA AGTAGAGGG CGGTAGACTA CTGTCACCTG TTAGACCTG ACGAGACAA CACAGBACG  
 126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L  
  
 901 TGAATTACTT CTATCCAGA GAGGCCAAG TACAGTGGAA GGTGGATAAC GCCCTCCAAAT CGGGTAACCT CCAGGAGAGT GTCACAGAGC AGGACAGCAA  
 ACTTATGAA GATAGGGTCT CTGGGTTC ATGTCACCTT CCACCTATTG CGGAGGGTA GCCATTGAG GTTGTGCTG TCTGTGCTT  
 160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K  
  
 1001 GGACAGCACC TACAGCCTCA GGAGCACCT GAGCTGAGC AAAGGAGCT AGCAGAAACA CAAAGTCTAC GCCTGGGAAG TCACCCATAA GGGCCTGAGC  
 CCTGTGCTGG ATGTGGGAGT CGTGTGGGA CTGCGACTCG TTTCGTCGTA TGCTCTCTG GTTTCAGATG CGGAGCTTC AGTGGGTAGT CCGGAGCTCG  
 193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S  
  
 1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTAAAT TAAATCCTCT ACGCCGGAGG CATTGCTGGCG AGCTGGTAC CGGGGATCT AGGCCTAAGC  
 AGCGGCGAGT GTTTCGAA GTTGTCCCT CTCACACATTA ATTAGGAA TGCGGCCCTGC GTAGCACCGC TCGACCCATG GGCCCTAGA TCCGGATG  
 226 S P V T K S F N R G E C O

Figure 21a

T C E T G T = S S f D D D D D

1201 CTCGGTTGCC GCGGGGGGT TTTATTTGTT GCGGACGGC ATCTCGAATG AACTCTGTCGC GCAGGTAGAA GCTTGGAGA TTATGGTCAC TGCAATGCTT  
 GAGCAACGG CGCCCGCAA AAAATAACAA CGGCTGCGG TAGAGCTTAC TTGACACAGG CGTCATCTT CGAAACCTCT AATAGCAGTG AGCTTACGAA  
 1301 CGGAATATGG CGCAAATATGA CCAAGAGCGG TTGATTGATC AGGTAGAGGG GGGCTGTCAG GAGTAAGC CCGATGCCAG CATTCTGAC GACCAACGG  
 GGTTATACC GGGTAACT GGTGTCGCC AACTAATCTAG TCCATCTCC CGCGCACATG CTCCATITG GGCTAACGGT GTAAAGACTG CTGCTATGCC  
 1401 AGCTGCTCG CGATTAGCTA AGAAAGTTAT TGAGCATCC TTGTCAGTA AAAGTAACTC TTTCACAG CTGTCATAAA GTTGTACCG CGAGACTTA  
 TCGACAGGC GCTAATGCT ATCTTCATAA ACTTCGAGG AGCAGCTAT TTTCATTTG AAAGTGTG CACAGTTT CAACGTGCC GGCTCTGAA  
 1501 TAGTCGCTTT GTTTTATTI TTAATGTTAG TTGTAATAG TAGGTAAGT CACGTAAAAA GGTTATCTAG AATTATGAG AAGAATATCG CATTCTCT  
 ATAGCGAAA CAAAATAAA AAATACATA AAATGATC ATGCGTCAA GTGCATTTT CCCATATGTC TTAAATAGC GTAAAGAGA  
 1 M K N I A F L L  
 ~STII signal TIR-1  
 ^Anti-VEGF Heavy Chain

1601 TGCATCTAG TTGTTTTCTGG CAGCTCTGG CTTATGCTAC AAACGCGTAC GCTGAGGTC AGCTGCTAC GGTGAGCTAG GGTCGGTGA GGCCTGGTGC AGCCAGGGG CTCACTCGT  
 AGCTAGATNC AGGCAAAAAA GATAACGATG TTGCGCATG CGACTCCAG TGACCCACT CAGACCGCCA CGGGACCAACG TCGGTCCCCC GAGTGAGCA  
 10 A S M F V F S I A T N A Y A E V Q L V E S G G G L V Q P G G S L R

1701 TGTCTCTGT CAGCTCTGG CTTATGCTAC ACCGACTACG GTATGACTAG GTATGACTAG GGTCGGTGA GGCCTGGTGA AGGGCTGTA AGGGCTGGGA TGGATTAACA  
 AACAGGACAC GTCGAGGAC GATGCTGAG TGCGTGTAGC CATACTGAC CCAGGAGTC CGGGCCAT TCCCGACCT TACCAACT ACCTAATGT  
 43 L S C A A S G Y D F T H Y G M N W V R Q A P G K G L E W V G W I N T  
 1801 CCTATACGG TGAACCGACC TATGCTGGG ATTCAAAAG TCCTTCACT TTTCCTTAG ACACCTCAA AGGACAGCA TACCTGCAGA TGAACAGCT  
 GGATATGCC ATTCGCTGG ATAGACGCC TAAGTGTGC AGCAAGTGA AAAGAAATTC TGTGGAGTT TTCCGCTGCT ATGACGCT ACTTGCGGA  
 77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L  
 1901 GCGCTGAG GACACTGCCC TTCTTAACTC CGTACTATTAC TGCAAAGTAC CGTACTATTAC CGGACACGAG CCACTGGTAT TTGACGCTT GGGTCAAGG AACCCGGTC  
 CGCGCACTC CTGTGACCGG AGATAATGAC AGTTTATG GGCATGATAA TGCGTGTCTC GGTGACCTA AAGTGCAGA CCCAGTTTC TTGGGCCAG  
 110 R A E D T A V P Y Y C A K Y P Y Y G T S H W Y F D V W G Q G T L V  
 2001 ACCGCTCTCT CGGCCCTAC CAAGGGCCA TGGCTCTTCC CCCTGGCACC CTCTCCAAAG AGCACCTCTG GGGGACAGC GGCCTGGC TGCCTGGCA  
 TGGCAGAGGA GCGGAGGTG GTTCCGGGT AGCCAGAAGG GGGACCGTGG GAGGAGGTTC TGTCGAGAC CCCCGTGTGG CGGGACCCG AGGGACAGT  
 143 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V K

2101 AGGACTACTT CCCGGAAAGC GTGACGGTGT CGTGGAACTC AGGACCCCTG AGCAGCCTG TGACACCTT CCCGGCTGTC CTACAGCTCT CAGGACTCTA  
 TCCTGATGAA GGGGTTGGC CACTGCCACA GCACCTGTAG TCCGCGGGAC CGGACGGGAG ATCGTGAAAC CCGGGGGTGT GGATGTCAGGA GTCTGCTAGAT  
 177 D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L Y

2201 CTCCCTCAGC AGCGTGGTGA CTGTCCTC TAGCAGCTG GGACCCAGA CCTACATCTG CAACGTGAAT CACAGCCA GCAACACAA GTGGGACAAG  
 GAGGGAGTCG TCGACCACT GAGACGGAG ATCGTGAAAC CCGGGGGTGT GGATGTCAGAC GTGTCAGTA GTGTCGGGT CGTTGTTGGT CCACCTGTC  
 210 S L S S V V T V P S S L G T Q T Y I C N V N H K P S N T K V D K

2301 AAAGTGTGAC CCAAATCTTG TGAACAAACT GACACATGCC CACCGTGGCC AGGACCTGAA CTCCCTGGGG GACCGTCACT CTCCTCTTC CCCCAAAAC  
 TTTCGAATCG GGTGTTAGAAC ACTGTGTTGA GTGTCAGGG TGTCGAGCTT GAGGACCCCG CTGCGAGTCA GAGGGAGAAG GGGGGTTTG  
 243 K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P K P

2401 CCAAGGACAC CCTCATGATC TCCGGACCC ATGCGTGGTGC GTGACGTCACT GACTCGAGTACG TACCGACCAAC GCGACGAGA CCCTGAGGTC AAGTTCAGTGG  
 GGTCTCTGTC GGATGTAATG AGGGCTTGGG GACTCGAGTACG TACCGACCAAC GCGACGAGA CCCTGAGGTC AAGTTCAGTGG  
 277 K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y V D

Figure 21b

2501 CGGGCTGGAG GTGCAATAATG CCAGACAA GCGCGGGAG GAGCAGTACA ACAGCACGTA CCGTGTGGTC AGCCTCCTCA CGTCCTGCA CCAGGACTGG  
 GCGCACCTC CACPATTAC GGTTCTGTT CGCGCCCTC CTGCAGTGT TGTCGTGAT GGACACAGA TCGCAGAGT GGCGAGAGT GGTCCTGACC  
 310 G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W

2601 CTGAATGCCA AGGAGTACAA GTGCAAGGTC TCCAACAAAG CCCTCCAGC CCCATCGAG AAAACCATCT CCAAAGCAA AGGCAGCCC CGAGAACAC  
 GACTTACGTT CCTCATGTT CACCTCCAG AGCTTGTT GGGAGGTGCG GGGTAGCTC TTGTTGTTA GTTGGTAA TCCCGTCGGG GTCTTGTGTT  
 343 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q

2701 AGGTGTACAC CCTGCCCA TCCTGGGAG AGATGACAA GAACAGGTC AGCCCTGACCT GCTGGTCA AGGCTCTAT CCCAGGACA TCGCCGTGGA  
 TCCACATSTG GGACGGGGT AGGCCCTTC TCTACTGGT CCTGGTCCAG TCGGACTGAA CGGACCACT TCCGAAGATA GGTCGCTGT AGCGCACT  
 377 V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E

2801 GTGGAGAGC AATGGCAGC CGGAGAACAA CTACAAGACC AGCGCTCCG TGCTGGACTC CGACGGCTC TCTCTCTT ACAGGAAGCT CACCGTGGAC  
 CACCTCTCG TTACCGTGC GCCTCTGG GTGTTGTTGTT GTGTTGTTG TGCGGAGGC ACGAACCTGAG GCTGCCGAGG AAGAAGAGA TGTCCTGCA GTGCACTG  
 410 W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D

2901 AAGAGCAAGT GGCAAGGG GAAGGTCTTC TGTGCTCG TGTGCTGAC AACCACTACA CGCAGAGAG CCTCTCCCTG TCTCGGGTAA  
 TCTCTGTCGA CGTCTCCCTCC CTTGAGAAG AGTACGAGG ACTACCTACT CGGAGACGTT TTGTTGATG TTGTTGATG GGTCCTCTC GGAGGGAGC AGGGCCCAT  
 443 K S R W Q G N V F S C S V M H E A L H N H Y T Q K S L S P G K

3001 AATAGATG CGACGCCCT AGAGTCCCTA ACCCTCGTT GCGCGGGC GTTTTTATT GTAACTCTAT GTTGTAGAGC TTATATCGA TAAGCTTA  
 TTATCGTAC GCTGCCGGGA TCTCAGGGAT TGGAGCTA CGGAGCCCA CAAAGAAATAA CAATGAGTA AATAGTAGCT ATTGAAATT  
 477 O

3101 TGGCTAGTT TATCACAGTT AAATGCTTA CGGAGTCTGG CACCGTGTAT GAAATCTAAC AATGCGCTIA TGTCATCCT CGGCACCGTC ACCCTGATC  
 ACCGCATCAA ATAGCTCAA TTAACTGATT GCTGCTAGT GCTGCTAGT GCTGGCACATA CTTTGTAGTG TTAGCGAGT AGCAAGTAGA GCCGTTGGCAG TGGFACTAC

^Start Tet Resistance Coding Sequence

3201 CTGTAAGGAT AGGCTGGTT ATGCCGGTAC TGCGGGCCT CTTGGGGAT ATCGTCCATT CGCACAGCAT CGCCAGTCAC TATGGGTGTC TGCTAGGCT  
 GAGATCCGTA TCCGACCAA TACGCCATG ACCGGCCCA TAGGAGTAA GAAACGCCCTA ATACCGCAG ATACCGCAG ACGATGCGA

3301

Figure 21c

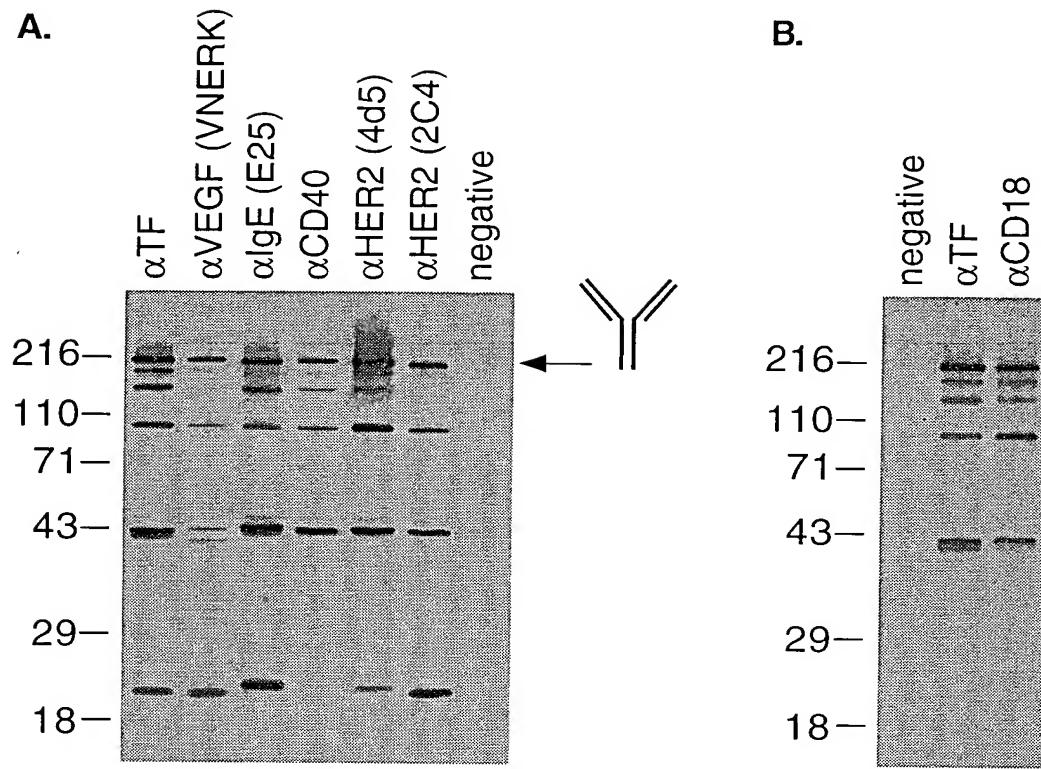


Figure 22